An update on indoor bioaerosols with emphasis on the fungi

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Definitions

- *__Bioaerosol__ - Population of airborne particles derived from living or dead organisms.*
- *__Organism__ - A living (or nearly living) creature, plant, fungus, or microorganism.*
- *__Bioagent__ – An organism, its parts, or excretions that can result in symptoms.*
- *__Reservoirs__ – Sites where bioagents are 'stored.'*
- ***Source** – site from which aerosols are produced.*

Fungal growth

- *Morphology*
- *Factors affecting growth*
- *Survival and dormancy*

What do fungi need for growth?

- *Water*
- *Nutrients*
- *Warmth*
- *Other factors*

- *Water must be continuously present*
- *Amount of water needed depends on*
  - *the kind of fungi*
  - *the kind of material used as food*
  - *temperature*

The aerobiological pathway

Source Factors →	**Aerosol Factors** →	**Exposure Factors** →	**Response factors**
•Organisms and agents • *physiology* • *biochemistry* •Populations • *interactions* • *dynamics* •Aerosol release	•Composition •*Dispersion* •Biological decay •Physical decay	•Time •Activity •Inhalation factors •Deposition, removal factors •Agent release and dispersion	•Cellular responses •Systemic responses •Dose factors •Immunol. •Toxicol.

Risk Assessment
Exposure Guidelines

- *Pathway complete: all factors support a cause/effect relationship*
  - *Agent is likely to be at least one of the contributing factors to disease*
  - *Other factors may play a crucial role*

- *Pathway incomplete: incomplete data*
  - *Agent may be at least one of the contributing factors to disease*
  - *Additional data is necessary*
  - *Other factors may play a crucial role*

- *Pathway incomplete: data indicate break in the pathway*
  - *Agent is unlikely to play a role in the disease outbreak*
  - *Other factors should be sought*

Fungus	*Glucan*	*Allergens*	*Mycotoxins*	*VOCs*
Stachybotrys	+++	++	*Satratoxin* *Roridin etc*	+?
Aspergillus	+++	*Asp f 1*	*Fumitrem.* *Ochratoxin* *Aflatoxin*	+++

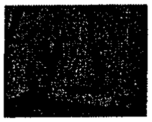
Fungal agents of disease

- ***Glucans***
  - *fungal cell wall components*
  - *endotoxin-like*
  - *irritants and immunostimulants.*
- ***Enzymes***
  - *released for "exo" digestion*
  - *Allergenic*
  - *Some may facilitate invasive disease*
- ***Secondary metabolites***
  - *Allergenic ?*
  - *Irritating, other effects? (e.g., volatile metabolites)*
  - *Toxic for some forms of life (e.g., mycotoxins, antibiotics).*

Mycotoxins

Fungus	Mycotoxin	Possible Health Effect

Aerosol and other exposure units:



- Fungal spores
- Fragments of spores
- Fragments of moldy building materials
- Resuspended dust
- Volatile organic compounds
- Offgassing chemicals from building materials
- High humidity
- Pests that like wet environments
- Bacteria
- Bacterial metabolites

Aerosol factors for S. chartarum

- *Composition/nature*
  - *Nature of particles*
    - *S. a. spores, mycelial fragments*
    - *Other spores contaminated with toxins*
    - *Other toxin-bearing particles*
    - *Volatilized toxins*
  - *Size of particles*
    - *spore aerodynamic diameter: 5-6um*
    - *size of toxin aerosol: unknown*

Aerosol factors for S. chartarum

- *Aerosol concentration dynamics*
  - *Physical decay*
    - *Unknown due to lack of particle size information*
  - *Biological decay*
    - *Do toxins change over time? Unknown*

Exposure factors for S. chartarum

- ***Time, activity:***
  - *Can be documented*
- ***Inhalation, deposition factors:***
  - *Physics well characterized for particles of known aerodynamic diameter; unknown for mycotoxins*
- ***Removal factors (from lung)***
  - *Unknown for S. chartarum spores or other toxin-containing particles*
- ***Toxin release and dispersion***
  - *Unknown for S. chartarum spores or other toxin-containing particles*

Dose/response considerations

- ***Amounts of toxin produced depends:***
  - *on fungal species and genetic pattern of the strain*
  - *on length of growing time*
  - *on kind of food, amounts of water and light*
  - *on temperature*
  - *on presence or absence of competition*
  - *on other unknown factors*
  - *All are interactive.*

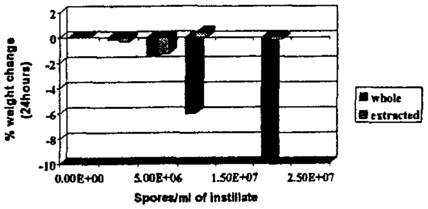
Toxin reaching affected organ system

- ***Product of:***
  - *# spores retained in the respiratory tract,*
  - *amount of toxin per particle,*
  - *the rate of toxin release from the particle, and*
  - *the rate that the toxin is removed from the site or destroyed.*

Amounts of toxins required for effect

- ***Known** - only from laboratory animal data; no human data*
- ***Known** - only for very large doses of inhaled or instilled toxin (no realistically low exposure studies).*
- ***Realistic** - chronic exposures have not been studied for any animal and certainly not for humans.*

Effects of spores on rat body weight



Human Data: Croft et al

- ***Symptoms***
  - *Dermatitis, memory loss,*
- ***Observation***
  - *documentation of toxin-producing* S. *chartarum strain; reasonable pathway for exposure*
- ***Authors conclusion***
  - *Stachybotrys toxins caused symptoms in couple likely to be heavily exposed*
- ***Comments***
  - *Man more heavily affected than woman; otherwise, hypothesis possible but not proven*

Auger et al

- ***Symptoms***
  - *Pseudo-chronic fatigue syndrome*
- ***Observations***
  - Penicillium brevicompactum *collected from home; removal apparently resolved symptoms*
- ***Authors conclusion***
  - *Some Penicillium toxin caused the problem*
- ***Comments***
  - *Other factors not considered? No documentation of level of exposure; no clear reason for blaming Penicillium; hypothesis not proven, unlikely*

Montana et al

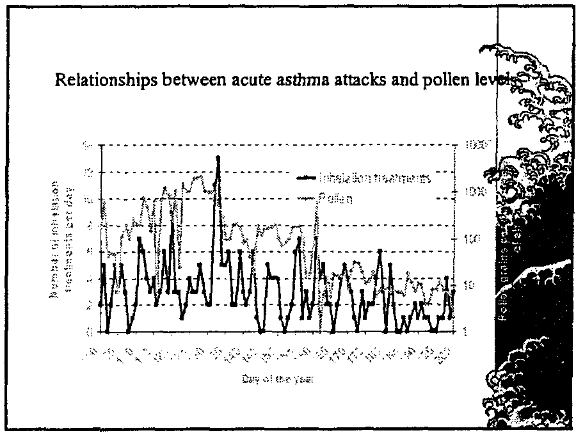
- ***Symptoms***
  - *Hemosiderosis*
- ***Observation***
  - *Documentation of toxin producing* S. *chartarum strain*
- ***Authors conclusions***
  - *Stachybotrys toxins' caused symptoms in babies*
- ***Comments***
  - *No mold or Stachybotrys in some affected children's homes; no logical pathway for exposure; hypothesis is not proven, and is unlikely*

The aerobiological pathway

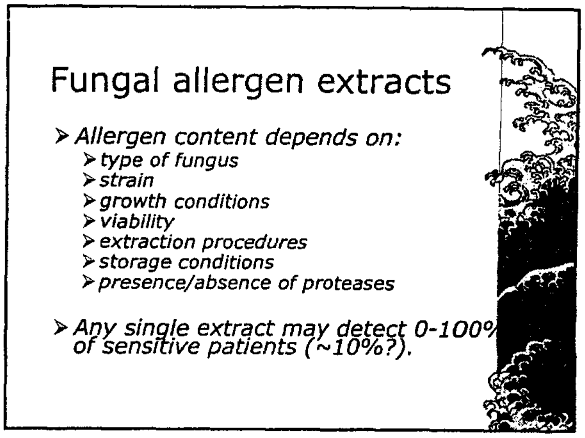
Source Factors	**Aerosol Factors**	**Exposure Factors**	**Response factors**
Fungi (and) S.chartarum present in most (not all houses)	None shown S.chartarum not in most air samples	No toxin exposure shown; ETS & drugs were common	Toxin may cause lung bleeding; would also cause nose rash, irritation, bleeding

Asthma

- *Reversible airway constriction*
- *Sensitization (setting up the system)*
- *Triggers leading to symptoms*

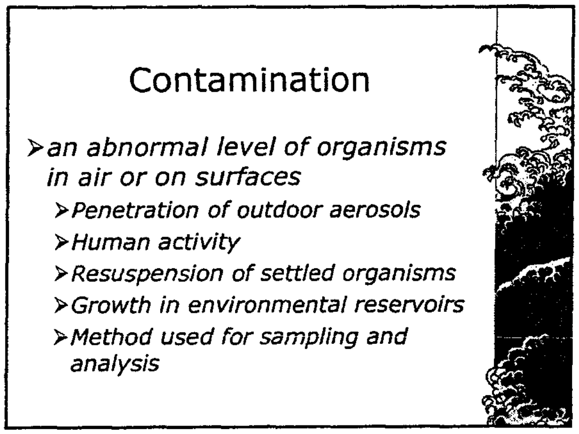


Relationships between acute asthma attacks and pollen levels



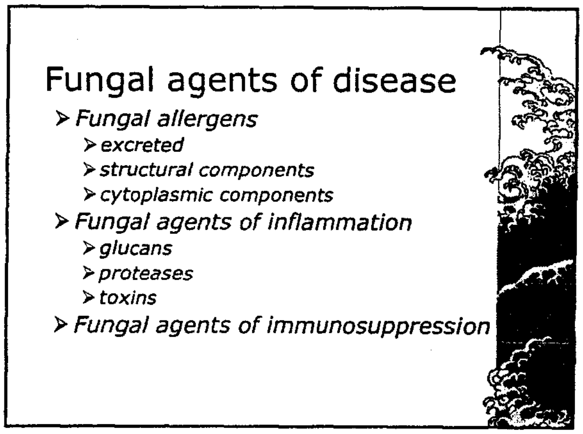
Fungal allergen extracts

- *Allergen content depends on:*
  - *type of fungus*
  - *strain*
  - *growth conditions*
  - *viability*
  - *extraction procedures*
  - *storage conditions*
  - *presence/absence of proteases*
- *Any single extract may detect 0-100% of sensitive patients (~10%?).*



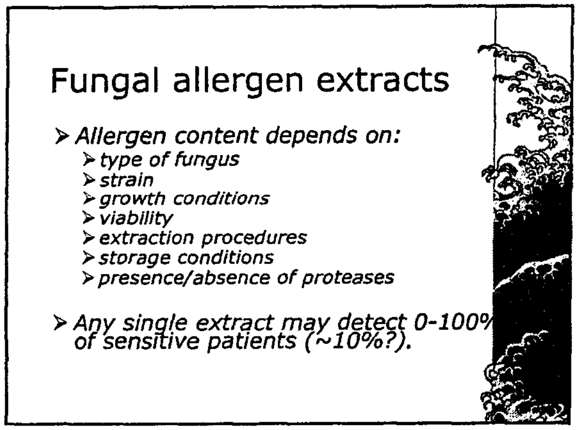
Contamination

- *an abnormal level of organisms in air or on surfaces*
  - *Penetration of outdoor aerosols*
  - *Human activity*
  - *Resuspension of settled organisms*
  - *Growth in environmental reservoirs*
  - *Method used for sampling and analysis*



Fungal agents of disease

- *Fungal allergens*
  - *excreted*
  - *structural components*
  - *cytoplasmic components*
- *Fungal agents of inflammation*
  - *glucans*
  - *proteases*
  - *toxins*
- *Fungal agents of immunosuppression*



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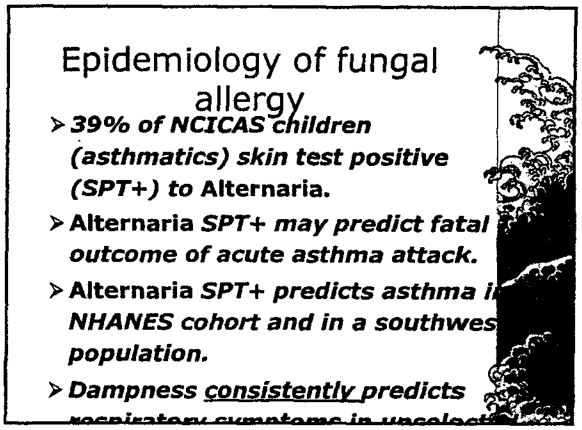


Epidemiology of fungal allergy

- ***39% of NCICAS children (asthmatics) skin test positive (SPT+) to* Alternaria.**
- **Alternaria *SPT+ may predict fatal outcome of acute asthma attack.***
- **Alternaria *SPT+ predicts asthma i NHANES cohort and in a southwes population.***
- ***Dampness consistently predicts***

Childhood respiratory symptoms and exposure to indoor fungal spores

Variable	*Relative Odds*	*P-value*
Cladosporium	**1.40**	**<0.025**
Yeast	**1.27**	**<0.05**
Epicoccum	**1.27**	**<0.1**

Documenting exposure/disease

Aspergillus fumigatus
outdoor air/ contaminated surfaces
air movement/filtration/dilution
inhalation/impaction
germination ↓
allergen release
asthma↓

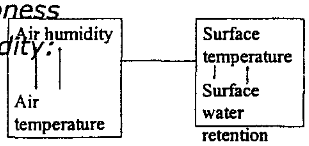
What do molds need for growth?

- *Water*
- *Nutrients*
- *Warmth*
- *Other factors*

- *Paper*
  - *wallpaper, wallboard, cardboard, ceiling tiles*
- *Sugars*
  - *fruits, vegetables, pastes, glues*
- *Fabrics*
- *Dust (skin scales)*
- *Wood*

Water and mold

- *Liquid water: available oxygen*
- *Wet surfaces: continuous wetting*
- *Damp materials: continuous dampness*
- *Humidity:*



Sporulation

- *Factors affecting spore production*
- *Morphology of spore production*
- *Spore release*
  - *Intrinsic*
    - *Basidiospores*
    - *Ascospores*
    - *Hyphomycetes*
  - *Activity-related*

Fungal aerosols

- *Particle sizes and shapes*
- *Viability*
- *Transport*
- *Removal*

Outdoor aerosols

- ➢*Ambient*
- ➢*Activity related*
- ➢*Exposure considerations*

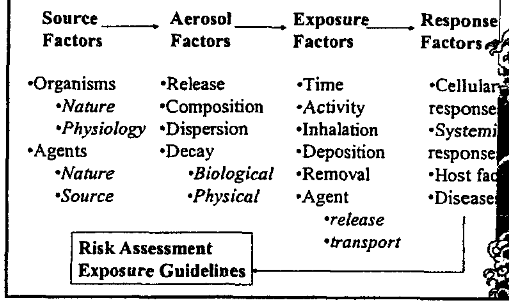
Indoor/outdoor relationships

- ➢*Penetration*
- ➢*Settling/reintrainment*
- ➢*Exposure considerations*

Indoor aerosols

- ➢*Dry interiors*
  - ➢*sources*
  - ➢*aerosol factors*
- ➢*Damp interiors*
  - ➢*sources*
  - ➢*aerosol factors*
- ➢*Wet interiors*
  - ➢*sources*
  - ➢*aerosol factors*

The aerobiological pathway



Source Factors → **Aerosol Factors** → **Exposure Factors** → **Response Factors**

Source Factors
- •Organisms
  - •*Nature*
  - •*Physiology*
- •Agents
  - •*Nature*
  - •*Source*

Aerosol Factors
- •Release
- •Composition
- •Dispersion
- •Decay
  - •*Biological*
  - •*Physical*

Exposure Factors
- •Time
- •Activity
- •Inhalation
- •Deposition
- •Removal
- •Agent
  - •*release*
  - •*transport*

Response Factors
- •Cellular response
- •Systemi response
- •Host fa
- •Disease

Risk Assessment
Exposure Guidelines

Developing an investigative strategy

- ➢*Map available information on the aerobiological pathway*
- ➢*Develop hypotheses*
- ➢*Determine crucial information gaps*
- ➢*Develop most efficient approach to filling the gaps*

Bioaerosol Investigations

- ➢*Use "visual" sampling wherever possible.*
- ➢*If you see contamination, it exists, and further sampling is rarely necessary as proof of its existence.*

Bioaerosol Investigations

- *Associate all sampling with specific reservoirs.*
- *Identify reservoirs, use bulk sampling to document contamination, use common sense to extrapolate exposure.*
- *Use before/after aggressive air sampling to document release from reservoirs.*

Bioaerosol Investigations

- *If you must collect "ambient" air samples for any reason:*
  - *Collect at least 10 samples/small site*
  - *Collect outdoor samples within 1 hour of each indoor set*
  - *Never try to prove the negative case with air sampling alone*

Bioaerosol Investigations

- *Before collecting any sample, develop a sampling plan that includes choice of an analytical method and choice of a laboratory to perform the analysis.*
- *CALL THE LABORATORY BEFORE BEGINNING THE SAMPLING!!!*

Measuring exposure 1

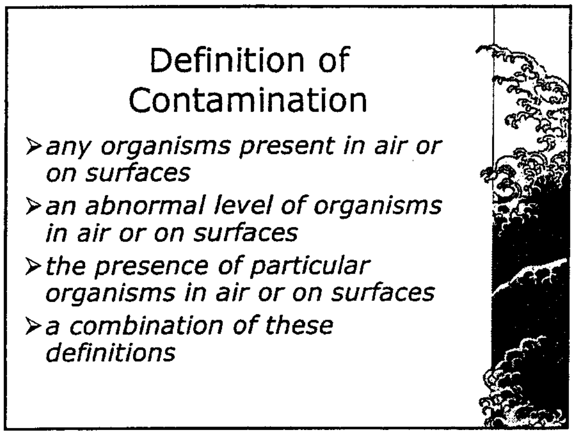
- *Indicator measurements*
  - *Conditions*
  - *Growth*
  - *Exposure*

Measuring exposure 2

- *Aerosol measurement*
  - *Particle counts*
  - *Sample collection considerations*
    - *Overall strategy*
    - *Sampling plans*
      - *sampler*
      - *sites*
      - *times*
      - *replicates*

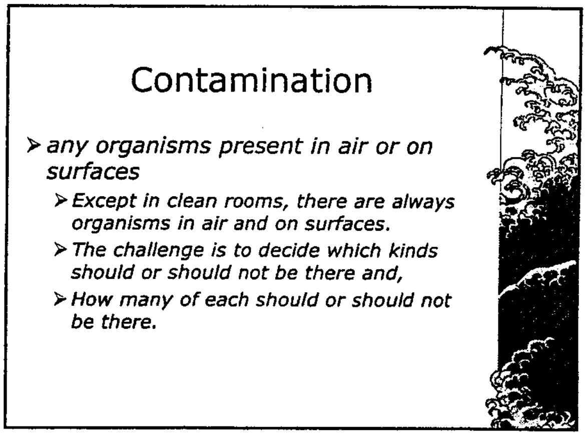
Data interpretation

- *Can we base interpretations on specific exposure/response information?*
- *Interpreting sampling data as "contamination"*
- *Interpreting reports*



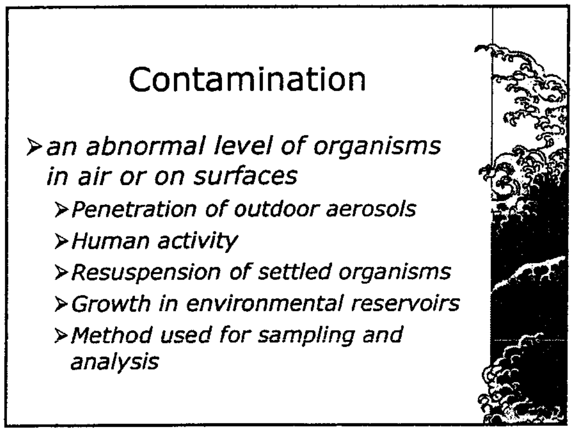
Definition of Contamination

- *any organisms present in air or on surfaces*
- *an abnormal level of organisms in air or on surfaces*
- *the presence of particular organisms in air or on surfaces*
- *a combination of these definitions*



Contamination

- *any organisms present in air or on surfaces*
  - *Except in clean rooms, there are always organisms in air and on surfaces.*
  - *The challenge is to decide which kinds should or should not be there and,*
  - *How many of each should or should not be there.*



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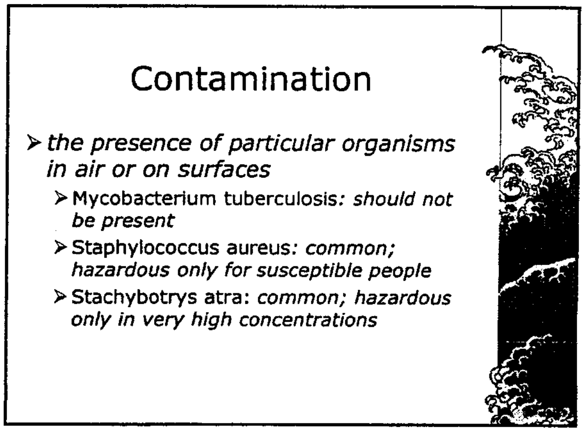
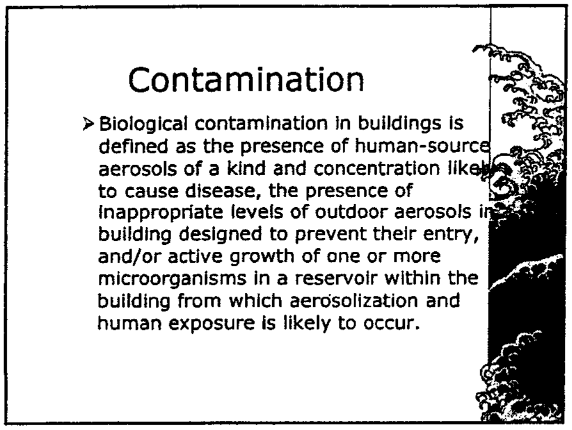


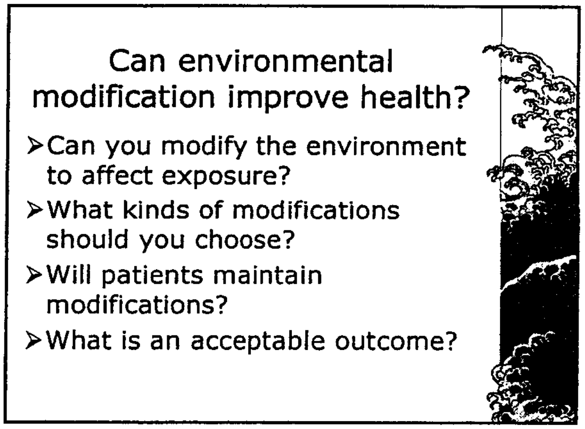
Contamination

- *the presence of particular organisms in air or on surfaces*
  - Mycobacterium tuberculosis*: should not be present*
  - Staphylococcus aureus*: common; hazardous only for susceptible people*
  - Stachybotrys atra: *common; hazardous only in very high concentrations*



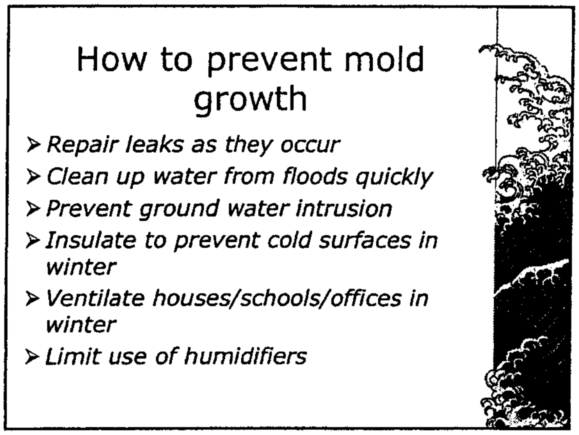
Contamination

- Biological contamination in buildings is defined as the presence of human-source aerosols of a kind and concentration like to cause disease, the presence of inappropriate levels of outdoor aerosols i building designed to prevent their entry, and/or active growth of one or more microorganisms in a reservoir within the building from which aerosolization and human exposure is likely to occur.



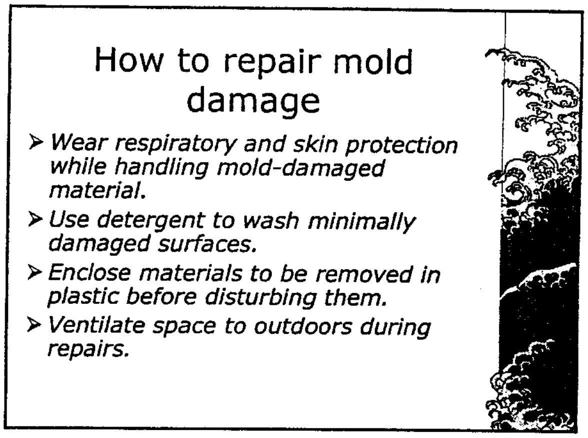
Can environmental modification improve health?

- Can you modify the environment to affect exposure?
- What kinds of modifications should you choose?
- Will patients maintain modifications?
- What is an acceptable outcome?



How to prevent mold growth

- *Repair leaks as they occur*
- *Clean up water from floods quickly*
- *Prevent ground water intrusion*
- *Insulate to prevent cold surfaces in winter*
- *Ventilate houses/schools/offices in winter*
- *Limit use of humidifiers*



How to repair mold damage

- *Wear respiratory and skin protection while handling mold-damaged material.*
- *Use detergent to wash minimally damaged surfaces.*
- *Enclose materials to be removed in plastic before disturbing them.*
- *Ventilate space to outdoors during repairs.*

Use Common Sense